REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments, remarks and enclosures herewith.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 40-51 were pending in this application and are under examination. Claims 40-50 have been amended herein, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

The Examiner is thanked for indicating that the finality of the previous Office Action has been withdrawn and that prosecution has been reopened.

It is respectfully submitted that the claims, herewith and as originally presented, are patentably distinct over the art, and that those claims are and were in full compliance with the requirements of 35 U.S.C. § 112. The remarks made herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112. Rather, the amendments and remarks herewith are made simply for clarification and to round out the scope of protection to which Applicant is entitled.

II. THE CLAIM OBJECTIONS ARE OVERCOME

Claims 40-41, 43-45 and 47 were objected to for allegedly failing to recite proper Markush language. In particular, the Examiner indicates that the claims recite "selected from the group comprising..." rather than "selected from the group consisting of".

Claims 40-41, 43-45 and 47 have been amended to recite proper Markush language.

Consequently, reconsideration and withdrawal of the objections is respectfully requested.

III. THE 35 U.S.C. §112 , SECOND PARAGRAPH, REJECTIONS ARE OVERCOME

Claims 40-51 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to claim the subject matter regarded as the invention. The rejection is respectfully traversed.

In particular, the Examiner indicates that it is not clear whether "in need thereof" limits the patient to be treated to those in need of treatment for a hyperproliferative disease of the skin or those in need of a pharmaceutical composition.

For clarity, claims 40-50 have been amended to recite "administering to a patient in need of treatment for a hyperproliferative disease of the skin" (claims 40, 41, 44 and 45), "administering to a patient in need of treatment for psoriasis" (claims 42, 46, 48 and 50), or "administering to a patient in need of treatment for psoriasis, acne vulgaris and hyperkeratosis" (claim 49).

Thus, Applicants respectfully submit that the claims are now clear. Reconsideration and withdrawal of the claim rejections is respectfully requested.

IV. THE 35 U.S.C. § 102 REJECTIONS ARE OVERCOME

Claims 40-43 and 48-51 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gottfried *et al.* Applicants respectfully traverse.

Applicants submit that in light of the amendments made to claims 40-43 and 48-51, which recite "administration to a patient in need of treatment of a hyperproliferative disease of the skin" or "psoriasis" or "psoriasis, acne vulgaris or hyperkeratosis" rather than a patient "in need thereof", which the Office Action interpreted to mean in need of a pharmaceutical composition, the art rejection is now moot. Applicants submit that Gottfried *et al.* does not teach or suggest administering a pharmaceutical composition to: (i) a patient in need of treatment of a hyperproliferative disease, as required by claims 40, 41, 44, and 45; (ii) a patient in need of treatment of psoriasis, as required by claims 42, 46, 48, and 50; or (iii) a patient in need of treatment of psoriasis, acne vulgaris, or hyperkeratosis, as required by claim 49. Therefore, Applicants submit that the subject matter of each of claims 40-43 and 48-51 is novel and thus meets the requirements of 35 U.S.C. § 102(b).

Accordingly, reconsideration and withdrawal of the claim rejections are respectfully requested.

V. THE 35 U.S.C. §103 REJECTIONS ARE OVERCOME

Claims 40-51 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Burchardt *et al.* (WO 97/15298; 1997). Applicants respectfully traverse.

The presently claimed invention pertains to the use of a pharmaceutical composition consisting of: (i) carbenoxolone; and (ii) one or more pharmaceutically acceptable carriers, diluents or excipients in the treatment of various hyperproliferative diseases. It would be clear to the skilled person that it is the carbenoxolone which is the biologically active component in the composition which treats the recited diseases, and not the carrier.

The Examiner contends that Burchardt *et al.* pertains to the use of carbenoxolone sodium and an LTD4 receptor antagonist, the latter of which the Examiner interprets to be a pharmaceutically acceptable carrier.

Applicants respectfully disagree for the following reasons.

The Examiner is respectfully directed to the case law, namely, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) in which it was held that "A patent need not teach, and preferably omits, what is well known in the art" *[Emphasis added]*. Thus, in view of the fact that the definitions of the terms "carrier", "diluent" and "excipient" are all well-known in the art, it should not be necessary to define them in the patent.

However, for the avoidance of doubt, it is submitted that carriers, diluents and excipients which have proven useful are well known in the pharmaceutical arts and are described in Remington: The Science and Practice of Pharmacy 1995, edited by E. W. Martin, Mack Publishing Company, 19th edition, Easton, Pa.

One of skill in the art would recognize that:

a "carrier" relates to an **inactive** compound which is combined with the active agent in a drug formulation, and is provided to facilitate administration of the formulation to a patient;

a "diluent" relates to an **inert** ingredient added to a pharmaceutical in addition to the active drug; and

an "excipient" relates to an **inactive** substance used as a carrier for the active ingredients of a medication.

Thus, it would be clear to the skilled person that carriers, diluents and excipients should not have any biological activity, and are merely included in a pharmaceutical composition to enable the active agent to be administered to the patient. In contrast, on page 3, lines 3-5 of Burchardt *et al*, it is clear that the LTD4 receptor antagonist is biologically active since it is a substance which blocks the biological effect of cysteinyl-leukotrienes LTC4 and LTD4 at their

receptor (CysLT1). Accordingly, the LTD4 receptor antagonist exerts its biological activity by blocking the leukotriene receptor, thereby preventing an associated signal cascade within the cell. Hence, in view of the well-known definitions of the terms "carrier", "diluent" and "excipient", and in view of the fact that an LTD4 receptor antagonist, is not biologically inactive (it exerts a strong biological effect by blocking signal transduction), Applicants respectfully submit that an LTD4 receptor antagonist cannot be defined as being a carrier, a diluent or an excipient.

Furthermore, on page 71 of the instant specification, the Applicants further discusses the well-known term "pharmaceutically acceptable carrier" as "being compatible with the other ingredients in the formulation and not injurious to the patient" and that it should be "biologically acceptable without eliciting an adverse reaction (e.g. immune response) when administered to the host". Such a definition is also well understood by those of skill in the art. As discussed below, Applicants submit that an LTD4 receptor antagonist elicits an immune response, and so cannot be defined as being a carrier, diluent or excipient. As taught on the paragraph spanning pages 1-2 of Burchardt *et al*, an LTD4 receptor antagonist is an anti-inflammatory biological, which is particularly suitable for the treatment of acute and chronic inflammatory processes, in particular for the treatment of inflammatory airway disorders such as asthma. Specifically, LTD4 receptor antagonists block the biological effect of the cysteinyl-leukotrienes LTC4 and LTD4 at their receptor (see Burchardt *et al* , page 3, lines 3-5), thus altering the immune response. Therefore, since an LTD4 receptor antagonist, by its nature and its design, elicits an immune response, it further prevents such a molecule from fitting the definition of a "pharmaceutical carrier" in accordance with the claimed invention and definitions known to those skilled in the art.

The Examiner has further asserted that the definition of a "pharmaceutically acceptable carrier" is non-limiting and does not preclude the use of an LTD4 receptor antagonist as a carrier. As discussed above, the well known definition of a carrier is one which is inactive, and which does not elicit an immune response. Applicant submits that LTD4 is an active agent and elicits an immune response, and so cannot be defined as a "pharmaceutically acceptable carrier", as required by the claimed invention. Hence, the term "pharmaceutically acceptable carrier" does preclude the use of an LTD4 receptor antagonist.

In addition, suitable indications for LTD4 receptor antagonist use are for the treatment and prevention of inflammatory disorders of the airway (see Burchardt *et al* page 6), and the

effects of using such a biological to treat hyperproliferative disorders of the skin, for example, Darier's disease, is not discussed and may, in fact, elicit an adverse reaction in a patient in need of treatment of a hyperproliferative disorder of the skin.

The Office Action states that a "patient in need thereof" has been interpreted to mean in need of treatment with the instantly claimed pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway, and accordingly, "the claims reasonably read upon the treatment of a patient in need of treatment with the claimed pharmaceutical composition", which the Office Action contends is "clearly met by the teachings of Burchardt *et al.*"

Applicants respectfully submit that the amendments to the claims, which clarify that the presently claimed method pertains to a patient in need of treatment for a hyperproliferative disorder of the skin, obviates the Examiner's rejection based on the initial interpretation of the claims.

Furthermore, as discussed above, Burkhardt *et al* pertains to the use of two active agents, i.e. (i) carbenoxolone sodium, and (ii) the LTD4 receptor antagonist, and not carbenoxolone alone, as required by the claims. Burkhardt *et al.* does not even hint at the notion that a single inhibitor of the retinoic acid biosynthetic pathway could be effectively used for treating the claimed hyperproliferative diseases. Thus, the skilled person would not have been motivated to use **only** carbenoxolone as the sole active agent in combination with one or more pharmaceutically acceptable carriers, diluents or excipients for treating the claimed hyperproliferative diseases. Moreover, the Applicants submit that the use of the combined formulation of carbenoxolone sodium, and a LTD4 receptor antagonist taught in Burkhardt *et al* could even elicit an adverse reaction in a patient in need of treatment of a hyperproliferative disorder of the skin. Accordingly, Burkhardt *et al* teaches away from the claimed invention, and it is therefore submitted that the use of only a single inhibitor of the retinoic acid biosynthetic pathway would not have been obvious to the skilled person.Therefore, for each of the foregoing reasons, namely: (i) that an LTD4 receptor antagonist cannot be considered a pharmaceutically acceptable carrier, (ii) that the claims specifically relate to methods that pertain to a patient in need of treatment for a hyperproliferative disorder of the skin, and (iii) that the skilled person would not have been motivated to use **only** carbenoxolone as an active agent to treat the recited

disorders, reconsideration and withdrawal of the rejections under §103(a) are respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to further examination and/or allowance, an interview with the is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments herewith and those of record, the application is in condition for allowance. Favorable reconsideration of the rejections of the application and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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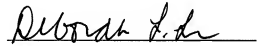
By: 

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